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| EXAMINER | |
|---|---|
| WEN, SHARON X | |
| ART UNIT | PAPER NUMBER |
| 1644 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/583,291 | UTKU ET AL. | |
| | Examiner | Art Unit | |
| | SHARON WEN | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *05 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *16,17 and 21-29* is/are pending in the application.

4a) Of the above claim(s) *16,17,21,23 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *22,24-26,28 and 29* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/16/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicant's amendment, filed 06/16/2006, has been entered.

Claims 1-15 and 18-20 have been canceled.

Claims 16-17, 21-29 are pending.

### *Election/Restrictions*

Applicant's election of Group II and species rheumatoid arthritis and intravenous in the reply filed on 10/05/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 16-17, 21, 23 and 27 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention/species, there being no allowable generic or linking claim.

Claims 22, 24-26 and 28-29 are currently under examination as they read on a method for preventing or treating rheumatoid arthritis comprising administering a fusion protein.

### *Drawings*

Figure 1 contains an amino acid sequence that is not accompanied by SEQ ID NO. Applicant is invited to label Figure 1 with SEQ ID NO: 1.

### *Claim Objections*

Claim 28 is objected to because it recites SEQ ID NO: 2. However, the application only has one sequence, SEQ ID NO: 1 as shown in Figure 1. Appropriate correction is required.

### *Information Disclosure Statement*

The information disclosure statement (IDS) submitted on 06/16/2006 has been considered by the examiner.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22, 25-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Regarding the instant claim limitations, the specification does not appear to provide an adequate written description for a genus encompassing any fragment of biliary glycoprotein (BGP) or any fragment of an immunoglobulin.

The instant specification describes the fragment of BGP as follow:

> In a particularly preferred embodiment, said biliary glycoprotein is a human biliary glycoprotein or a fragment thereof. In one embodiment the CEACAM1 protein or peptide conjugate of the present invention comprises at least a fragment of the amino acid sequence shown in FIG. 1. Active fusion proteins could be larger or smaller than the ones specifically described here. While the present fusion protein described are of about 233 amino acids, fusion proteins containing a number of amino acid residues, e.g., up to about 50 or 100 amino acid residues or more, that contain the described fusion protein, portions thereof, or similar fusion protein may have biological activity as well. Similarly, fusion proteins smaller than those shown in FIG. 1 may also have similar biological activity. Similarly, fusion proteins with amino acid substitutions or other alterations may block the activities of the described fusion protein or the parent molecules. Cyclic or otherwise modified forms of the fusion protein would also be expected to have biological activity. Preferably, the fusion protein of the present invention have about 233+/-5 to 10 amino acids derived from CEACAM1 protein. (see paragraph [0039]).

Applicant discloses that the extracellular domain of BGP is 1 to 228 residues of SEQ ID NO:1 which has the required activity of the claimed fusion protein. Beyond the reliance upon the disclosed species, there is insufficient structural information or defining characteristics, which provide for a sufficient written description of the genus of BGP fragments that are capable of modulating immune cell activation, proliferation or differentiation, a feature deemed essential to the fusion protein.

The standard for Written Description is met by "showing that an invention is complete by disclosure of sufficiently detailed, **relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure**, or some combination of such characteristics." See Enzo Biochem., Inc. v. Gen-Probe Incorporated 323 F.3d 956 (Fed. Cir. 2002).

In the instant Application, there is insufficient written description to lead a person of skill in the art to know which sequences are essential, which sequences are non-essential, for the BGP fragments to modulate immune cell activation, proliferation or differentiation or binding of CEACAM1 to its ligand.

Similarly, there is insufficient written description to lead a person of skill in the art to know which fragments are essential, which fragments are non-essential, for the immunoglobulin fragments to attribute to the fusion protein activity of modulate immune cell activation, proliferation or differentiation because the specification only supports the Fc portion of the immunoglobulin as part of the fusion protein (see, e.g., paragraph [0048]).

The instant claims do not provide sufficient structural and functional characteristics coupled with a known or disclosed correlation between function and structure because the disclosure fails to describe the common attributes or characteristics that identify members of the genus of fragments BGP or immunoglobulin, known and unknown at the time the invention was made.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.) Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision. (See page 1115.)

Applicant is invited to amend the claims to recite the extracellular domain of CEACAM1 as the fragment of BGP and Fc portion of the immunoglobulin as the fragment of immunoglobulin (as recited in claim 28) in order obviate this rejection.

Claims 22, 24-26 and 28-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a therapeutic agent for sepsis, does not reasonably provide enablement for a preventive and/or therapeutic agent for any disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

With regards to the instant claims, their breadth, the state of the prior art, and the lack of guidance provided by the inventor, comprise the primary issues as regards the unpredictability of the claimed method.

The present claims are drawn to a method of preventing or treating rheumatoid arthritis (RA) comprising administering a CEACAM1-Fc fusion protein.

The specification provides showed that CEACAM1-Fc fusion protein reduced human PBMC proliferation, inhibited IFN-gamma production and mouse splenocyte proliferation, all *in vitro* (see Examples 1-3 and Figures 1-4).

However, beyond the disclosure mentioned above, the specification does not provide sufficient *in vivo* or *in vitro* evidence showing that the fusion protein is effective in treating or preventing any disease, in particular, RA.

One of skill in the art is well-aware that RA is difficult to treat or prevent. According to *Smolen et al.,* the cause of RA remains unknown and many factors have been identified to play a role in the pathogenesis of RA which involves a complex of

immune response (see page 1861, Pathogenesis of rheumatoid arthritis). However, the instant disclosure does not provide sufficient in vitro or in vivo evidence showing the administration of the fusion protein comprising can counter-act the cause or the manifestation of RA as defined in order to effectively treat or prevent the disease.

Applicant appears to rely on the in vitro data for the present claimed method of treating for preventing RA. However, it is noted that pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of *Ex parte Aggarwal*, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Beyond the in vitro data, the specification does not adequately teach how to effectively prevent or treat RA or reach an appropriate beneficial therapeutic endpoint by administering the fusion protein. The specification does not teach how to extrapolate data obtained from various in vitro observations with the fusion protein to the development of effective methods of preventing or treating RA.

There is insufficient guidance and direction as well as objective evidence provided for treating the scope of diseases encompassed by the claimed method.

In view of the lack of predictability of the art (e.g., treating and prevention RA) to which the invention pertains, undue experimentation would be required to practice the claimed method of treating and prevention RA with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively use the claimed agent and absent working examples providing evidence which is reasonably predictive that the claimed agent is effective for treating or preventing RA commensurate in scope with the claimed invention.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON WEN whose telephone number is (571)270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571)272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sharon Wen/
Examiner, Art Unit 1644
January 28, 2010